



# Anthropogenic nutrients and harmful algae in coastal waters



Keith Davidson <sup>a,\*</sup>, Richard J. Gowen <sup>b</sup>, Paul J. Harrison <sup>c</sup>, Lora E. Fleming <sup>d,e</sup>,  
Porter Hoagland <sup>f</sup>, Grigorios Moschonas <sup>a</sup>

<sup>a</sup> Scottish Association for Marine Science, Scottish Marine Institute, Oban, Argyll PA37 1QA, UK

<sup>b</sup> Fisheries and Aquatic Ecosystems Branch, Agriculture Food and Environmental Science Division, Agri-Food and Biosciences Institute, Newforge Lane, Belfast BT9 5PX, UK

<sup>c</sup> Department of Earth & Ocean Sciences, University of British Columbia, Vancouver, BC V6T 1Z4, Canada

<sup>d</sup> European Centre for Environment and Human Health, University of Exeter Medical School, RCHT Knowledge Spa, Truro, Cornwall TR1 3HD, UK

<sup>e</sup> Oceans and Human Health Center, University of Miami, Miami, FL 33149, USA

<sup>f</sup> Marine Policy Center, MS#41, Woods Hole Oceanographic Institution, Woods Hole, MA 02543, USA

## ARTICLE INFO

### Article history:

Received 12 April 2014

Received in revised form

1 July 2014

Accepted 3 July 2014

Available online

### Keywords:

Harmful algal blooms

HABs

Anthropogenic nutrients

Human health

Economic impact

## ABSTRACT

Harmful algal blooms (HABs) are thought to be increasing in coastal waters worldwide. Anthropogenic nutrient enrichment has been proposed as a principal causative factor of this increase through elevated inorganic and/or organic nutrient concentrations and modified nutrient ratios. We assess: 1) the level of understanding of the link between the amount, form and ratio of anthropogenic nutrients and HABs; 2) the evidence for a link between anthropogenically generated HABs and negative impacts on human health; and 3) the economic implications of anthropogenic nutrient/HAB interactions. We demonstrate that an anthropogenic nutrient-HAB link is far from universal, and where it has been demonstrated, it is most frequently associated with high biomass rather than low biomass (biotoxin producing) HABs. While organic nutrients have been shown to support the growth of a range of HAB species, insufficient evidence exists to clearly establish if these nutrients specifically promote the growth of harmful species in preference to benign ones, or if/how they influence toxicity of harmful species. We conclude that the role of anthropogenic nutrients in promoting HABs is site-specific, with hydrodynamic processes often determining whether blooms occur. We also find a lack of evidence of widespread significant adverse health impacts from anthropogenic nutrient-generated HABs, although this may be partly due to a lack of human/animal health and HAB monitoring. Detailed economic evaluation and cost/benefit analysis of the impact of anthropogenically generated HABs, or nutrient reduction schemes to alleviate them, is also frequently lacking.

© 2014 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/3.0/>).

## 1. Introduction

Phytoplankton form the base of the aquatic food chain. In marine waters, there are approximately 4000 species of phytoplankton (Sournia, 1995), most of which are benign to humans. Some species are considered “harmful” however, impacting human and animal health through the production of a variety of potent natural biotoxins, and/or by causing economic losses through their negative impacts on human uses of ecosystem services (Anderson et al., 2002; Davidson et al., 2011; Hallegraeff, 1993).

Harmful species are present within most phytoplankton classes, but a distinction should be made between the impacts caused by

high versus low biomass HABs. High biomass HABs while sometimes toxic (Black, 2001) more often result in oxygen depletion in bottom waters when a bloom sinks and is decomposed by bacteria. Farmed (and wild) fish may also be killed by the smothering of gills due to phytoplankton mucus production or from gill abrasion by spines on the cell walls of some phytoplankters (Bruno et al., 1989). In contrast, low biomass HABs (≈ a few hundred to thousands of cells/L) threaten human health (and the health of other animals) as a result of the biotoxins produced by these phytoplankters being concentrated by filter feeding shellfish and other organisms that may subsequently be ingested by humans or transferred through the marine food web (Davidson et al., 2011). Humans may also be exposed to, and affected by, biotoxin-contaminated water or aerosols (Bean et al., 2011).

Several researchers (Anderson, 1998; Smayda, 1990; Van Dolah, 2000) have reported an apparent global increase in HABs in marine

\* Corresponding author. Tel.: +44 1641 559256; fax: +44 1631 559001.

E-mail address: [kda@sams.ac.uk](mailto:kda@sams.ac.uk) (K. Davidson).

waters. Coupled with an increasing demand for seafood products, such an increase would imply that HABs pose important global health and economic risks.

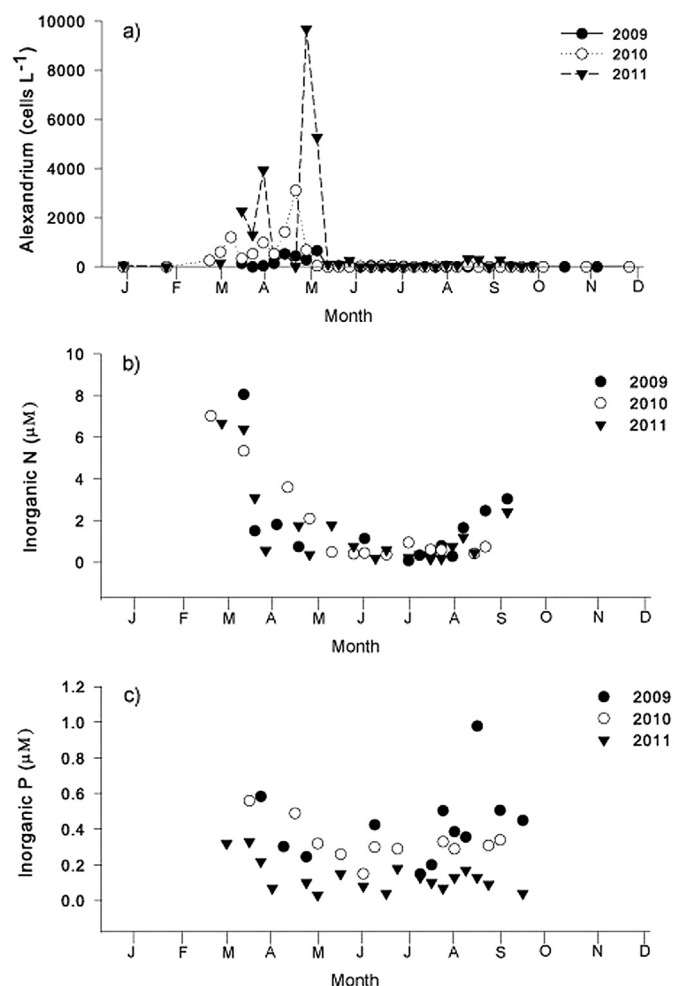
Determining the causative factors for HAB events is complex. While the ballast water transport of cells (Smayda, 2007) and climate change (Hallegraeff, 2010; Moore et al., 2008) are potentially important in governing the biogeography and formation of HABs, it is generally accepted that the availability of dissolved inorganic nutrients likely mediate phytoplankton growth in most coastal waters (Howarth and Marino, 2006). As increases in human coastal populations, industrialization, and the intensification of agriculture have elevated the supply of nitrogen (N) and phosphorus (P) to coastal waters (Ferreira et al., 2011), the role of anthropogenic nutrient enrichment and associated changes in nutrient ratios are among the most frequently proposed and debated hypotheses relating to increased HABs in coastal waters (Glibert et al., 2005; Harrison et al., 2012; Heisler et al., 2008; Smayda, 1990).

Whether elevated concentrations of these nutrients are accompanied by HABs is not straightforward, as determining cause and effect is difficult. Therefore while the link between anthropogenic nutrients, harmful algae and both human health consequences and economic impact remains debated within the “HAB research community”, many other scientists, managers and members of the public erroneously believe this link to be globally established. In this paper we therefore explore the strength of this link and ongoing areas of uncertainty, with the aim of providing better understanding of the issue for those who seek to make coastal management decisions.

## 2. Eutrophication, nutrients, and HABs

Fertilizers, sewage, animal wastes, atmospheric inputs, and coastal aquaculture all contribute to elevated nutrient concentrations in coastal waters, with strong evidence that elevated nutrients have led to increased phytoplankton biomass and primary production in some locations (Anderson et al., 2008; Gowen et al., 2012; Heisler et al., 2008; Smayda, 1990). Clearly, the appearance of HABs could be regarded as an undesirable disturbance, and hence HABs and incidents of high seafood toxicity have been used to “diagnose” eutrophication (Foden et al., 2010).

While a link between anthropogenic nutrient enrichment and HABs is often assumed to be widespread, the relationship is complex because HABs are not a new phenomena, and they may occur naturally with a wide geographical distribution that predates the enrichment of coastal waters, clearly demonstrating that anthropogenically-caused enrichment is not a prerequisite for their occurrence (Richardson, 1997). For this reason, and because other pressures such as climate change can influence HABs (Hallegraeff, 2010; Moore et al., 2008), the occurrence of HABs does not necessarily imply eutrophication. Recent examples of HABs with no identified anthropogenic link include *Karenia mikimotoi* blooms in NE Atlantic coastal waters (Davidson et al., 2009) and *Alexandrium fundeyense* in the Gulf of Maine (Anderson et al., 2008). Another example of a location that suffers HAB events with no clear anthropogenic link is Loch Creran on the west coast of Scotland where blooms of the paralytic shellfish poisoning causative genus *Alexandrium* occur. This area exhibits relatively low nutrient concentrations with few anthropogenic inputs (Fehling et al., 2006; Lønborg et al., 2009). However, as demonstrated by Fig. 1, *Alexandrium* blooms in Loch Creran differ markedly in magnitude between years (a near 20-fold difference in peak cell abundance between 2009 and 2011). The location is not subject to significant anthropogenic nutrient loading and while the *in situ* nutrient concentrations

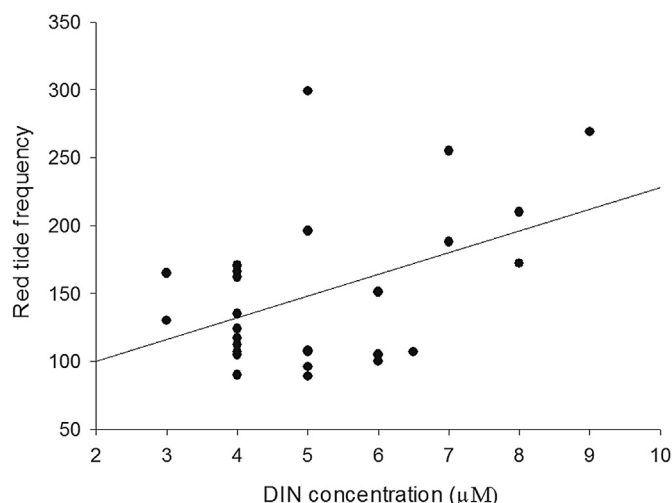


**Fig. 1.** Time course of: a) potentially harmful (saxitoxin producing) *Alexandrium* sp. cell abundance b) inorganic N and c) inorganic P in Loch Creran Scotland during the summers of 2009–2011.

were similar in different years, a dramatic bloom of *Alexandrium* occurred in 2011 alone.

Nevertheless, scientists have argued (Gowen et al., 2008; Hays et al., 2005) that eutrophication may be implied by either the occurrence of HABs where none have occurred before, or by increases in HAB frequency or HAB spatial/temporal extent that can be tied to anthropogenic nutrient enrichment. Consequently, in a European context Ferreira et al. (2011) recommended that, if, but only if, HAB frequency, amplitude, or toxicity increase in response to nutrient inputs, then HABs should be treated as one of the Marine Strategy Framework Directive (MSFD) indicators of eutrophication.

We may also ask whether eutrophication is always accompanied by HABs. This is a more equivocal question, because determining a cause and effect relationship is often difficult. While regulatory or human health based monitoring programmes are increasingly generating HAB time series, those that include parallel environmental information are less common, with sufficiently long time series (e.g. longer than a decade) of nutrient loading and taxonomic data that allow natural inter-annual variability to be quantified rarely available (Hays et al., 2005). Notwithstanding this problem, where data exist, a number of studies provide strong support for the hypothesis that anthropogenic nutrients have increased the occurrence of HABs in some coastal regions. Prominent amongst these are studies of Tolo Harbour in Hong Kong and Japan's Seto



**Fig. 2.** The frequency of red tides in the Seto Inland Sea versus dissolved inorganic N concentration (DIN) from 1973 to 2000. A statistically significant linear relationship ( $P = 0.02$ ) is evident. Data are from Imai et al. (2006).

Inland Sea. As discussed by (Gowen et al., 2012), for inner Tolo Harbour, there is *prima facie* evidence that anthropogenic nutrient enrichment caused an increase from ~3 to 30 red tide events during the eight year period from 1982 to 1989 (Hodgkiss and Ho, 1997). Time series of HABs in the Seto Inland Sea of Japan (Imai et al., 2006; Nishikawa et al., 2010) and associated changes in nutrient loadings and concentrations also provide evidence for an anthropogenic nutrient-driven increase in the frequency of HABs on a larger spatial scale than inner Tolo Harbour (Gowen et al., 2012, Fig. 2).

Results in other regions do not demonstrate a clear nutrient enrichment – HAB linkage. For example, many researchers have linked the “appearance” of blooms of the foam-producing nuisance flagellate *Phaeocystis* in the southern North Sea to anthropogenic nutrients (Anderson et al., 2002; Hallegraeff, 1993; Smayda, 1990). While the suggestion that *Phaeocystis* appeared where none existed before is incorrect (Cade and Hegeman, 2002; Gowen et al., 2012), there is convincing evidence that enrichment increases the duration of spring *Phaeocystis* blooms in the Dutch and Belgian coastal waters (Cade and Hegeman, 1986, 2002). Nevertheless, similar enrichment in the inner German Bight at Helgoland has not been shown convincingly to support HABs, most likely because of an over-riding hydrodynamic influence (Hickel, 1998). Furthermore, recent studies in the southern North Sea suggest that *Phaeocystis* blooms are related to large scale water movements and climatic conditions (Breton et al., 2006; Gieskes et al., 2007).

For many other coastal regions, the HAB-nutrient enrichment debate is ongoing, with insufficient evidence to draw definitive conclusions. For example, a significant correlation exists between decadal increases in paralytic shellfish poisoning (PSP) toxins in Puget Sound, with the expansion of local coastal human populations (Trainer et al., 2003) suggesting that pressures, such as nutrient enrichment associated with human population growth, influence an increase in HAB frequency. However, Trainer et al. (2003) pointed out the possible link to decadal scale climate variation and Moore et al. (2008) argued that increasing water temperature may be driving the increase in PSP. Arguments have also been presented both for and against the stimulation by nutrients of blooms of the neurotoxic dinoflagellate *Karenia brevis*, in the Gulf of Mexico (Anderson et al., 2008; Olascoaga et al., 2008; Vargo et al., 2008). Similarly, while nutrient enrichment has been suggested as a potential cause of the increase in HABs in Korean waters, Kim

(2010) finds that the mechanisms of initiation and development of blooms of important species, such as the fish killing dinoflagellate *Cochlodinium polykikoides*, are poorly understood due to inadequate information about oceanographic conditions in the Western Pacific and East China Sea.

### 3. Nutrient ratios

The intracellular and extracellular balance of nutrients is central to phytoplankton growth and competition (Tilman, 1977). Therefore, an important issue related to HABs is the role of nutrient ratios in governing their bloom formation. In marine systems the “Redfield Ratio” concept has long been central to the debate surrounding resource competition. Redfield demonstrated that the chemical composition of plankton tends towards an average atomic C:N:P ratio of 106:16:1. The nutrient in least supply relative to the requirements for growth (determined by their biochemical composition) is deemed the “limiting” nutrient (Davidson et al., 1992) with the important caveat that if both nutrient concentrations are high with respect to a phytoplankton’s requirement, the ratio will have little or no effect. The switch between different forms of nutrient limitation is thought to follow a threshold response. Thus the Redfield N:P ratio is widely used with respect to ambient concentrations of dissolved inorganic N and P to infer which nutrient is likely to limit a phytoplankton population, with ratios of <16:1 and >16:1 indicating N and P limitation, respectively.

An anthropogenically mediated change in the N:P ratio (rather than their absolute concentrations) has frequently been linked to the appearance of HABs, known as the “nutrient ratio hypothesis” (Hodgkiss and Ho, 1997; Smayda, 1990). However, such a link is increasingly being challenged on theoretical grounds in freshwater (Reynolds, 1999; Sterner and Elser, 2002). In marine systems in particular, (Flynn, 2010) argues that phytoplankton growth on N and P is related to their intracellular concentration (the cell quota, (Droop, 1968)), and hence models based on extracellular nutrient concentrations are flawed. Moreover, different species have no physiological basis for a fixed intracellular nutrient ratio (Davidson et al., 1991; Geider and La Roche, 2002), and hence will exhibit different critical N:P ratios, that may differ from Redfield values that are basin and season wide averages. Understanding the role of species specific nutrient ratios may therefore be key to the application of nutrient competition theory (Elser et al., 2007) to HABs.

While suitable field data sets to test the nutrient ratio-HAB hypothesis are rare, those key examples that do exist (from the North Sea (Riegman et al., 1992), and Hong Kong waters (Hodgkiss and Ho, 1997)) are often quoted in support of a N:P-HAB link, in apparent contradiction of the theoretical arguments above. However, close examination of these studies (below) suggests that the links between HABs and nutrient ratios are tenuous.

In the Marsdiep region of the Dutch Wadden Sea, the total N:P ratio decreased from 38 to 13 during the 1970s and 1980s. It has been hypothesised that this increased the magnitude and duration of summer *Phaeocystis* blooms (Riegman et al., 1992), but the large number of often contradictory studies does not provide a clear picture, particularly as mistaken assertions that *Phaeocystis* blooms first appeared in this location in the 1970s (Hallegraeff, 1993; Smayda, 1990) incorrectly implied a link with N:P ratio. Subsequently (Phillipart et al., 2007) suggested that while it is not possible to preclude a role for nutrient ratios in partly controlling the Dutch coastal phytoplankton community, other factors may be important or dominant, with the drivers of long term fluctuations in *Phaeocystis* in the southern North Sea remaining unclear.

In Tolo Harbour, Hong Kong, the N:P ratio decreased from ~20 to 10 from 1982 to 1989 because of increased sewage loads. This

decrease is significantly correlated with an increase in HAB events (Hodgkiss and Ho, 1997), but is only based on an 8-year time-series. After sewage diversion in 1998, the N:P ratio increased to ~35:1 from 1998 to 2007. However, a decrease in HAB frequency started in 1991, prior to the sewage diversion (Harrison et al., 2012) and this lower frequency was unaffected by the diversion (Fig. 3). The lack of a clear link is potentially due to the main red tide organism in Hong Kong waters being the heterotrophic dinoflagellate *Noctiluca scintillans* that grazes mainly on diatoms, and is therefore only indirectly connected to nutrients. Moreover, physical factors have increasingly been demonstrated to influence red tide events in Hong Kong waters and the number of typhoons (and hence hydrodynamic stability) potentially explains the differences between the number of red tides in different years in Tolo Harbour (Wong et al., 2009).

The above discussion has concentrated on N and P. However, one important phytoplankton class, the diatoms, also require silicon (Si) to build their cell wall. The potential for diatom Si limitation is exacerbated by low Si concentration in sewage effluent and agricultural runoff, with a low Si:N ratio potentially promoting dinoflagellates (Davidson and Gurney, 1999; Officer and Ryther, 1980), a group that contains relatively more harmful species. Prominent examples of anthropogenically elevated N:Si ratios include the southern North Sea, German Bight, and Baltic Sea (Gieskes et al., 2007; Hickel, 1998; Humborg et al., 2008). As Si is used structurally, it cannot be redistributed easily within phytoplankton cells, and therefore the consequences of its low availability are different than N and P, with theoretical models suggesting that extracellular concentrations are important in governing growth rate (Flynn and Martin-jézéquel, 2000). While most field studies confirm that Si limitation promotes flagellates over diatoms, definitive evidence that HAB species, other than the nuisance *Phaeocystis*, prosper under these conditions is lacking (Tett et al., 2003). Hence, the assertion that changing N:Si will promote HABs is based on the likelihood that a dinoflagellate-dominated phytoplankton assemblage contains more HAB species, rather than any specific evidence for the creation of ecological niches favouring HAB species.

Nutrient ratios have also been suggested to influence the production of toxins by some HAB species. Much of the evidence in

support of this hypothesis comes from laboratory studies that demonstrate elevated toxicity when one nutrient becomes limiting and growth slows. While evidence exists for a wide variety of species, the most comprehensive studies are related to *Pseudo-nitzschia* (Fehling et al., 2004a, 2004b; Pan et al., 1996; Wells et al., 2005) and *Alexandrium* (Granéli et al., 1998; John and Flynn, 2002; Murata et al., 2006; Taroncher-Oldenburg et al., 1999) responsible for amnesic and paralytic shellfish poisoning, respectively. Such studies imply that blooms are likely to exhibit elevated toxicity towards their ends, but does not help to explain the suggested widespread increase in HABs in the last few decades.

#### 4. Hydrodynamics

In a number of the examples above physical conditions have been highlighted as potentially important or over-riding factors in the control of HAB occurrence/magnitude. Other examples include the Gulf of Mexico where wind speed has also been shown to influence *Karenia brevis* blooms (Stumpf et al., 2009) and the Baltic Sea where the surface accumulation of cyanobacteria is promoted by calm weather (Kanoshina et al., 2003). Such physical factors may also be key to the geographical inconsistency in the influence of anthropogenic nutrient enrichment on HABs, as rates of lateral exchange, mixing, or dispersion within and between water bodies differ (Gowen et al., 2012).

Hydrodynamics may act in a range of ways. Factors such as the strength of vertical mixing and its consequences for the illumination experienced by phytoplankton are important, and spatio-temporal patterns in stratification also influence phytoplankton species succession. Solar warming of the sea surface, or the input of freshwater, create surface layers of lower density water. Hence, while nutrient inputs to such layers (either natural or anthropogenic) may stimulate blooms, biomass can be diluted or removed through dispersion by currents or the consumption by planktonic and benthic animals. Strong vertical mixing, due to wind, tidal currents, or surface cooling, also carries phytoplankton away from the surface light, and can suspend large quantities of light-obscuring sediment from the seabed in shallow areas.

Different hydrodynamic features of water bodies provide an explanation for why HABs occur in some enriched waters, but are

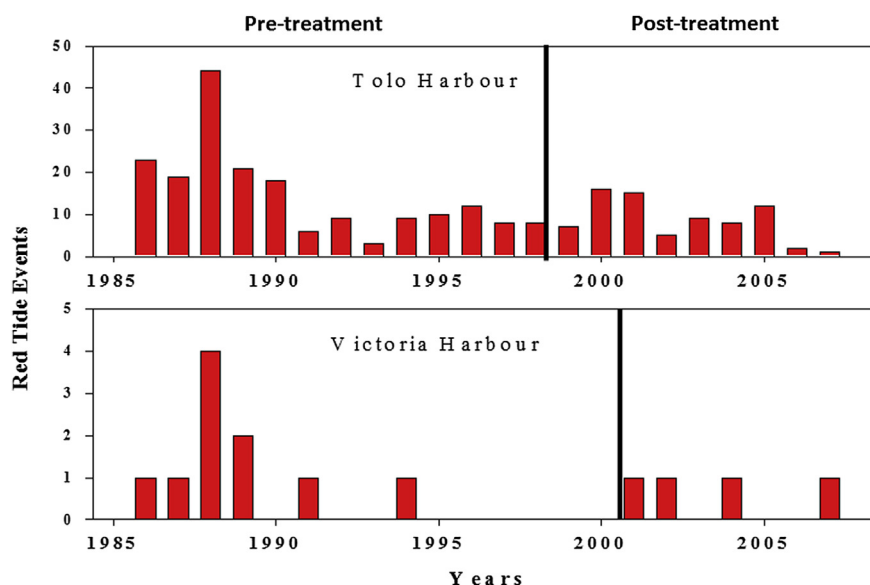


Fig. 3. The number of red tide events in Tolo Harbour and Victoria Harbour (Hong Kong) from 1986 to 2007 (see Harrison et al. (2012)). The vertical lines indicate the time of sewage diversion at each location. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



less frequent or absent in others. High biomass blooms, sometimes including blooms with harmful consequences are a feature of Tolo Harbour in Hong Kong (Xu et al., 2010), Loch Striven on the Scottish west coast (Tett et al., 1986)(Tett et al., 1986), and the Seto Inland Sea of Japan. In contrast, the enriched but energetic waters of Victoria Harbour, Hong Kong (Xu et al., 2010), Carlingford Lough, on the border between Northern Ireland and the Republic of Ireland (Capuzzo, 2011), and the eastern Irish Sea (Gowen et al., 2008) do not exhibit the symptoms of eutrophication. This is because their hydrodynamic characteristics (i.e., rapid flushing in Victoria Harbour, and tidal stirring in Carlingford Lough and the Eastern Irish Sea) counteract nutrient enrichment, reducing the potential for development of high biomass HABs. The influence of hydrodynamics on nutrient/HAB linkage can be illustrated by comparison of the nutrient enriched Victoria and Tolo Harbours of Hong Kong. High flushing rates normally reduce stratification in Victoria Harbour, resulting in lower chlorophyll biomass (Fig. 4) and less frequent red tides than other enriched locations in the same region (Fig. 3). Only when summer stratification occurs do chlorophyll concentrations approach those in the more permanently stratified Tolo Harbour.

## 5. Type of nutrient

The different forms of nutrients that are available may also influence HAB development. While most of the focus has been on inorganic nutrients, there are significant pools of dissolved organic N and P (DON and DOP) in coastal waters (Antia et al., 1991), originating from both allochthonous and autochthonous sources (Davidson et al., 2007; Glibert et al., 2005; Pete et al., 2010). Increasing evidence suggests that organic nutrients promote the growth of some HAB species including, PSP-causing dinoflagellates such as *Alexandrium* spp. (Leong et al., 2004), the hepatotoxic *Prorocentrum minimum* (Heil et al., 2005), the brown tide chrysophyte *Aureococcus anophagefferens* (Glibert et al., 2007) and the amnesic shellfish poisoning (ASP) causative diatom, *Pseudo-nitzschia* (Loureiro et al., 2009). In addition, some key harmful genera, such as the diarrhetic shellfish poisoning (DSP) causing-dinoflagellate *Dinophysis*, feed heterotrophically on organic matter (Minnhagen et al., 2011; Park et al., 2006), see section 6 below.

Urea has often been identified as an organic N form of concern (Glibert et al., 2006). Recently, urea use has increased markedly and, while regionally variable, urea now accounts for greater than 50% of global nitrogenous fertilizer usage (Glibert et al., 2006), with

urea concentrations in some coastal waters being enhanced significantly through the terrestrial runoff of unutilized fertilizer. Urea may be an important N source for phytoplankton (Solomon and Glibert, 2008; Solomon et al., 2010), even in non-enriched locations. For example, between 24 and 44% of phytoplankton N uptake at the chlorophyll maximum in Loch Creran during summer 2010 was urea-N, even though its concentration in the water column never exceeded 1  $\mu\text{M}$  (Fig. 5).

Association between HABs and urea fertilizer usage has been suggested (Glibert et al., 2006) based on global maps of urea use and HAB distributions, but the lack of long term time-series studies of HABs and their toxins prior to changes in fertilization practices, as well as the lack of observed non-HAB events, currently prevents definitive conclusions from being drawn. Utilisation of urea has been demonstrated for a number of important HAB organisms (Cochlan et al., 2008; Collos et al., 2007; Probyn et al., 2010; Sinclair et al., 2009). Glibert et al. (2008) also showed that, of 13 surveyed species, urease activity was greatest in two (harmful) dinoflagellates, but as urease activity of some of the diatoms studied exceeded that of other harmful dinoflagellates, the results are not clear cut.

The laboratory based *Alexandrium tamarens* data of Leong et al. (2004) is sometimes used as evidence that the toxin concentrations in urea-grown dinoflagellates exceed that of nitrate-grown cells (e.g. Glibert et al. (2008)). However, Leong et al. (2004) pointed out that toxicity “did not vary dramatically”, and indeed that ammonium grown cells generated the highest toxicity (Fig. 6). The work of Xu et al. (2012) further illustrates the difficulty in determining the role of urea in HAB development. These authors found the growth dynamics and toxicity of *Alexandrium tamarens* and *Alexandrium catenella* to differ with different forms of N and P; and for *A. tamarens*, ammonium-grown cells to generate the highest cellular toxin content, nitrate-grown cells the highest toxin production rate, and urea-grown cells the highest growth rate.

An influence of enhanced concentrations of coastal N through fertilizer derived urea, rather than other N species is therefore possible, but unambiguous data to demonstrate the species affected, geographical locations, and magnitude or form (growth rate, toxicity, etc.) of any effect are still lacking. A better understanding of the competition for urea between harmful and benign phytoplankton would help to clarify and quantify any specific anthropogenic urea-HAB link. Detailed local interpretation and analysis of nutrient loading data are also required. For example, the British Survey of Fertiliser Practice 2011 (Holmes, 2012) indicates

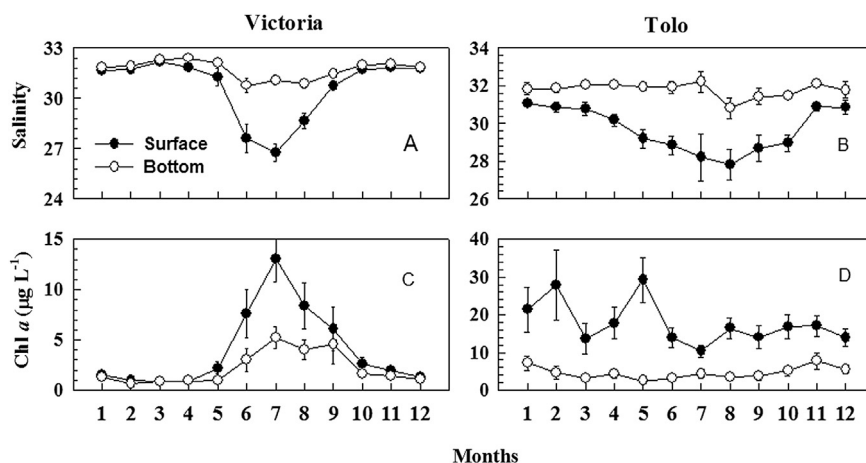


Fig. 4. Monthly mean surface and bottom salinity in a) Victoria Harbour and b) Tolo Harbour (Hong Kong). Monthly mean phytoplankton biomass estimated by chlorophyll a (Chl a) in c) Victoria Harbour and d) Tolo Harbour (from Xu et al. 2010).

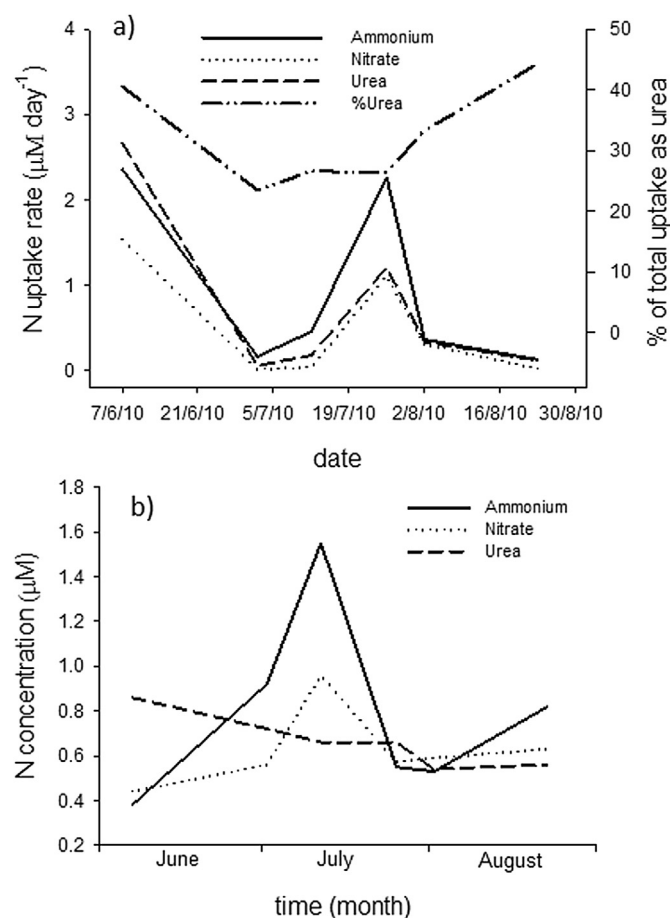


Fig. 5. a) The rate of uptake of ammonium, nitrate, and urea along with the percentage of total N uptake that was urea, in Loch Creran, Scotland, in summer 2010 determined by  $^{15}\text{N}$  uptake. b) The concentrations of ammonium, nitrate and urea at the same (10 m) depth that the uptake experiments were conducted.

that 358,000 tonnes of urea were used as fertiliser in that year; this was 7.4% of the total, with urea ammonium nitrate (UAN) contributing another 7.2%. However, most of this fertiliser was applied in the months of March, April and May, which is before the main season for dinoflagellate growth.

## 6. Mixotrophy

The role of nutrients in promoting HABs is further complicated by the increasing realization that many phytoplankters are capable of combining both phototrophic and heterotrophic modes of nutrition in what is termed mixotrophy (Jones, 1997; Stoecker, 1998). Recent reviews (Burkholder et al., 2008; Glibert and Legrand, 2006) have highlighted the importance of different forms of heterotrophic nutrition for a rapidly increasing list of HAB species. Examples of osmotrophs include *Aureococcus anophagefferens* brown tides in coastal waters of Long Island and bays of Maryland (Glibert et al., 2007), with heterotrophy now thought, based on laboratory studies, to support organisms including the important diarrhetic shellfish poisoning causative genus, *Dinophysis* (Minnhagen et al., 2011). Notwithstanding the above examples, a full understanding of the role of mixotrophy in promoting harmful blooms is lacking, with the relative importance of photosynthesis, dissolved organic nutrients, ingestion of prey, and the factors that govern the partitioning of these nutritional modes by both HAB and benign organisms being largely unknown (Burkholder et al., 2008; Montagnes et al., 2008).

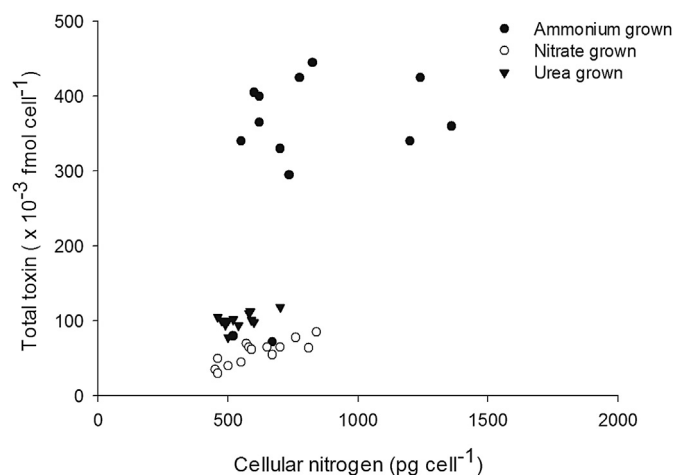


Fig. 6. The relationship between cellular N content and total toxin for *Alexandrium tamarense* grown separately on ammonium, nitrate and urea (redrawn from Leong et al., 2004).

## 7. Implications for human health

The relationship between HABs, their biotoxins, and negative impact on human health has been long understood (Gowen et al., 2012). However, although the number of recorded HAB events has been increasing, there is no documented parallel increase in human and other animal health events (with the possible exception of the freshwater cyanobacteria, Zaia et al., 2010). Because the link between anthropogenic nutrients and HAB events is not universal, it is difficult to point to HAB-related human health incidents that are the consequence of anthropogenic nutrient enrichment. The lack of any clear link is most likely because most HAB observations result from HAB monitoring programs only designed to ensure shellfish safety. This also implies that harvesting closures based on monitoring appear to have been generally successful in preventing contaminated shellfish from reaching the market.

Blooms of species that produce biotoxins (Table 1), regardless of their cause, are of concern from a human and animal health perspective. Humans and animals encounter these toxins through a range of mechanisms, such as direct water ingestion or contact, aerosolized transport, or the consumption of a marine organism that has concentrated the toxins through filter feeding (e.g., shellfish) or through the food chain (e.g., fish). Most known algal toxins are neurotoxins, although some can cause skin and liver damage and even cancer. The majority of human diseases associated with HAB toxins appear to be acute phenomena, although some (e.g., ciguatera fish poisoning) can cause prolonged sub/chronic disease, and the chronic aspects of HAB diseases have been poorly studied (Fleming et al., 2011; Okamoto and Fleming, 2005; Zaia et al., 2010).

While the threat posed by cyanobacterial toxins from inland and brackish coastal waters to animals, and to a lesser extent to humans, has been recognized by some medical and public health practitioners, the risk associated with marine biotoxins is less well appreciated, likely leading to an under-reporting and under-recording of seafood poisonings. A recent study of medical data from Wales (Hinder et al., 2011) demonstrated very low numbers of recorded shellfish poisonings but also that it was impossible to verify the number of affected individuals who do not seek medical treatment.

Even in coastal areas where HABs are endemic and there is a requirement for medical reporting of HAB-associated diseases (e.g. ciguatera fish poisoning and neurotoxic shellfish poisoning in

**Table 1**  
Major HAB organisms associated with human health effects (adapted from [Zaias et al., 2010](#)).

Representative HAB organism	Biotoxins	Vector/route(s) of exposure	Human health effect/illness
Diatoms			
<i>Pseudo-nitzschia</i> spp.	Domoic acid	Shellfish Fish <sup>a</sup>	Amnesiac shellfish poisoning (ASP)
Dinoflagellates <i>Gymnodinium catenatum</i> , <i>Pyrodinium bahamense</i> var. <i>compressum</i> , <i>Alexandrium</i> spp.	Saxitoxins	Shellfish Pufferfish	Paralytic shellfish poisoning (PSP)
<i>Dinophysis</i> spp., <i>Prorocentrum lima</i>	Okadaic acids	Shellfish	Diarrhetic shellfish poisoning (DSP)
<i>Prorocentrum minimum</i>	Neurotoxins	Shellfish Fish <sup>a</sup>	Venerupin shellfish poisoning (VSP) <sup>a</sup>
<i>Karenia brevis</i> (formerly <i>Gymnodinium breve</i> )	Brevetoxins	Shellfish  Fish <sup>a</sup>  Aerosols	Neurotoxic shellfish poisoning (NSP) Neurotoxic fish poisoning <sup>a</sup> Florida red tide respiratory irritation
<i>Azadinium</i> spp.	Azaspiracids	Shellfish	Azaspiracid shellfish poisoning (ASP)
<i>Gambierdiscus toxicus</i> , Possibly <i>Ostreopsis</i> spp.; <i>Coolia</i> spp.; or <i>Prorocentrum</i> spp.	Ciguatoxins	Fish	Ciguatera fish poisoning (CFP)
Cyanobacteria <i>Microcystis</i>	Microcystins	Water Aerosols <sup>a</sup> Fish <sup>a</sup>	Liver damage Liver cancer
<i>Lyngbya</i>	Lyngbyatoxins	Water	Skin irritation

<sup>a</sup> Vectors/effects that remain open to scientific debate.

Florida, USA), under-diagnosis and under-reporting still occurs ([McKee et al., 2001](#); [Watkins et al., 2008](#)). This situation is even worse for the illnesses associated with HAB biotoxin-contaminated aerosols and water, such as the respiratory irritation and exacerbation of asthma linked to brevetoxin aerosol exposure during HABs of *Karenia brevis* and related organisms ([Fleming et al., 2011](#)).

Major issues in documenting the possible human (and animal health) impact of HABs include the lack of systematic surveillance and baseline incidence rates for HAB-associated human illnesses, both locally and globally. Furthermore, detection methods for HAB toxins in the environment and more importantly, in humans, are either completely lacking (particularly human biomarkers), or expensive and not widely available ([Backer and Fleming, 2008](#); [Kite-Powell et al., 2008](#)). Recent efforts by the US Centers for Disease Control and Prevention [CDC] and other organizations to establish a coordinated human, animal, and environmental health surveillance network known as the Harmful Algal Bloom-related Illness Surveillance System (HABISS) (<http://www.cdc.gov/hab/surveillance.htm>) may improve this situation in the future.

Given both the difficulties of establishing cause and effect relationships and the lack of systematic and consistent medical recording and public health reporting, it is not surprising that there are no clear links between anthropogenic nutrient-generated HABs and human health effects in marine waters. Yet our understanding

of the potential for HABs to harm health is now much greater than it was only 20–30 years ago. This potential is evident from the documented increasing worldwide incidence of cyanobacterial blooms in freshwater bodies that have been associated with nutrient enrichment and linked to reports of deaths and illnesses of domestic and other animals, although demonstrating increased incidence of human health events has been more difficult ([Stewart et al., 2011](#); [Zaias et al., 2010](#)), as is the quantification of the future scale of any nutrient-HAB health problem.

## 8. Prevention, control and economic impacts

Strategies to limit sewage, agricultural and industrial discharges to coastal waters are being implemented in many countries by P and N removal from waste and control of fertilizer application. Proper assessment of the ecological effects and economic costs of this approach is typically lacking (but see [Lancelot et al., 2011](#)). Furthermore, nutrient removal is expensive and may not have the effect of reducing the frequency and magnitude of HABs or their economic impacts.

As with health effects, the economic impacts of HABs can be attributed to anthropogenic factors only if a causal link can be shown to exist between them. Economists arguably have paid relatively more attention to high-biomass blooms (cf. [Soderqvist, 1998](#); [Taylor and Luongo, 2009](#)), with the economic and coastal management literature offering few examples of economic damages arising from anthropogenic nutrient-driven low-biomass, toxic algal blooms.

Much of the extant literature on the economic impacts of HABs has employed relatively crude measures and methodologies, the results of which often are difficult to compare (see [Hoagland et al., 2002](#)). For example, in the United States, a purported \$50-million annual loss attributed to paralytic shellfish poisoning in Bering Sea surf clams (*Spisula polynyma*) has been misrepresented repeatedly by policy-makers, as there is no evidence that such a fishery is commercially viable ([Hoagland, 2008](#)). Therefore, there is a need for research to understand the consequences of HAB events associated with changed recreational activities, fishery closures, or reductions in market supplies for different locations and for different groups of people.

While several rigorous studies of the economic effects of HABs do exist ([Jin and Hoagland, 2008](#); [Morgan et al., 2009](#); [Nunes and van den Bergh, 2004](#); [Parsons et al., 2006](#); [Scatista, 2004](#); [Wessells et al., 1995](#)), these studies have not demonstrated clear links to anthropogenic nutrients. For example [Anderson \(2000\)](#) reported on the economic impact of HAB in coastal waters of the US and gave examples of the economic loss due to large blooms of *Alexandrium fundyense* in New England. However, such blooms are a natural occurrence and there is no evidence of an anthropogenic nutrient driven increase in their magnitude or frequency of occurrence.

A rough estimate of the economic effects of HABs in the United States is \$100 million per year (at the 2012 value of the dollar). [Anderson et al. \(2000\)](#) estimated the proportional breakdown of costs related to HAB impacts to be: 45% for public health costs, 37% in term of the costs of closures and losses experienced by commercial fisheries, 13% to the impact on lost recreation & tourism, and 4% to monitoring and management costs.

A comparable estimate for the European Union (EU) is an order of magnitude larger at \$1 billion annually; although approximately two-thirds of this is associated with the noxious, but non-toxic, effects of macroalgal (and some microalgal, e.g., *Phaeocystis*) blooms affecting the human uses of the coast ([Hoagland and Scatista, 2006](#)). Most other parts of the world report only *ad hoc* estimates of impacts, stemming from extraordinary events (e.g.

Anderson, 2003). From an economic perspective, the demonstration of a nutrient-low biomass HAB link would influence the array of policy responses, thereby adding the regulation of nutrients from point or non-point sources as potentially feasible responses.

The economic effects of HABs arise from public health costs including morbidities and mortalities, commercial fishery closures and fish kills, declines in coastal and marine recreation and tourism, and the costs of monitoring and management. Aggregating economic effects both within and across these categories can be problematic, as the measures of effects are rarely the changes in economic surpluses sought by economists (Hoagland et al., 2002). Estimates of these effects should (but often do not) attempt to account for how humans tend to react when faced with a bloom: beach-goers choose another beach, commercial shell-fishermen another fishery, and seafood consumers another protein (Morgan et al., 2010). Although exceptions exist, including the so-called “halo effect” by which broader markets are adversely influenced as a consequence of the miscommunication of risks (e.g., Parsons et al., 2006 on the *Pfiesteria* spp. case), the economic effects of HABs tend to be localized (Hoagland et al., 2009; Jin et al., 2008; Morgan et al., 2009; Scatista et al., 2003).

Even if a reduction in HABs can be achieved the economic understanding of the relative costs of HAB mediated “harm” and preventative measures is currently poor. Japan’s Seto Inland Sea provides an example where the economic impacts of (high biomass) HAB events arguably have been tied to anthropogenic sources of nutrients. Fig. 7 displays a time series of the lost sales from local aquaculture operations, as estimated by the Japan Fisheries Agency (Imai et al., 2006). The straight line is a linear fit, suggestive of a slight downward trend, although it cannot explain the substantial variability in the data. If the outlier year of 1972 is ignored, lost sales have remained fairly constant over time, averaging  $\$10.5 \pm \$5.5$  million per year over 35 years (~95% confidence interval), even as pollution regulations have been implemented.

The reasons for continuing impacts in the Seto Inland Sea relate to the succession of HABs dominating a system characterized by changing anthropogenic nutrient loading. During the last two decades pollution controls have been implemented on a consistent basis, leading to a highly modified, oligotrophic system (Yamamoto, 2003). Therefore, while the overall frequency of high biomass HABs has been reduced through nutrient control measures, some HAB species have increased (Imai et al., 2006), with biotoxin-producing

species now causing problems through their ability to compete in low phosphorus conditions.

Gren et al. (1997) conducted a seminal study of the net benefits of simulated nutrient reductions to control eutrophication and associated cyanobacterial blooms in the Baltic Sea, finding that the benefits of a 50% reduction in N and P input was roughly proportional to the control costs for the Baltic as a whole, with significant variation in net benefits depending upon the implementing jurisdiction. However, the potential for complex feedbacks between oxygen, phosphorus, and nitrogen may cause the ecosystem to respond in unexpected ways, rather than producing a shift back to a hypothesized pre-impacted condition (Vahtera et al., 2007).

One comprehensive study of the costs and potential ecological effectiveness of nutrient reduction strategies is that of Lancelot et al. (2011) who used a modelling approach to evaluate the impact of *Phaeocystis* blooms in the southern North Sea. They found the costs of nutrient reduction-based *Phaeocystis* mitigation to be substantial and dependent of the scale of reduction in bloom magnitude/duration desired. Evaluating the economic benefit and ecological implications of such reductions remained uncertain, however, preventing a cost-benefit analysis from being conducted.

Measures to prevent or to mitigate the effects of HABs, whether they are related to anthropogenic nutrients or not, are increasingly topical (Anderson, 2009, 2004). Many methods of bloom control have been proposed, including mechanical, biological, chemical, genetic, and environmental. While successful examples of local control measures exist, for example the use of clay dispersal to control blooms of *Cochlodinium polykrikoides* in Korean waters (Kim, 2010); these measures are frequently too rudimentary, localized, or problematic for widespread implementation (Anderson, 2009). Hence, monitoring rather than control is likely to remain the most useful HAB management strategy. Monitoring, however, is not a cheap option, with significant costs having to be borne by governments and/or industry (Anderson et al., 2001). Therefore, given the uncertainty in the anthropogenic nutrient-HAB relationship and the difficulties in assigning a value to HAB-related “harm,” there is a critical need for increased attention to economic assessments of their effects and the choices of management responses.

## 9. Conclusions

A link between anthropogenic nutrients and HABs is clear in some of the studies described above, but other examples demonstrate that this link is not universal. Hence, the role of anthropogenic nutrients in promoting HABs is location-specific and most frequently associated with high biomass organisms, but with hydrodynamic conditions and other pressures often over-riding nutrient effects at local scales. Evidence from key examples used in support of the nutrient ratios – HABs hypothesis is unconvincing, and while organic nutrients, and urea in particular, are increasingly being shown to play a role in supporting the growth of phytoplankton, a clear demonstration that HAB species and/or their toxicity are specifically promoted by anthropogenic urea remains elusive. Verification of this link is particularly important, because its clear demonstration would have significant implications for terrestrial farming practices and regulation in the developing world, where urea fertilizer use has become increasingly prevalent.

While the potential human health effects of some HAB species are clear, with the exception of freshwater cyanobacteria, negative health impacts from anthropogenic nutrient-generated HABs have not been well established, perhaps because nutrients are linked more clearly with high biomass species rather than low biomass biotoxin-producing organisms. Nutrient reduction strategies in anthropogenically enriched waters may be beneficial in terms of

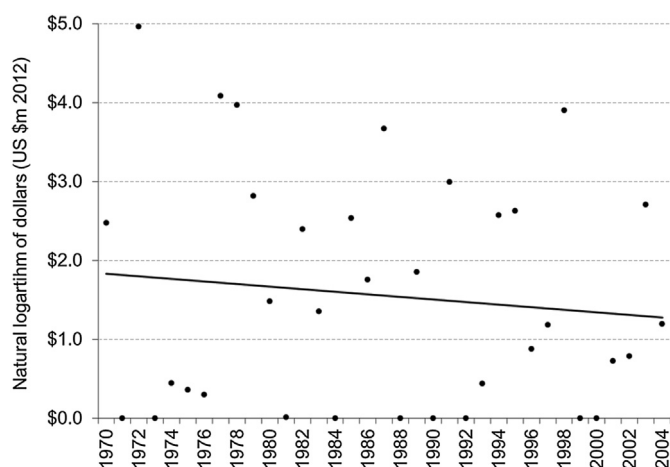


Fig. 7. Time series of estimated lost sales (gross revenues) from aquaculture operations in Japan's Seto Inland Sea during 1970–2004. Estimates are expressed as the natural log of millions of 2012 US dollars. Source: after Imai et al. (2006) citing Japan Fisheries Agency studies.



reducing the undesirable effects of eutrophication such as bottom water deoxygenation and fish kills. However, given the uncertain outcomes of how the composition of the phytoplankton community will respond, the lack of human biomarkers and surveillance data on HAB health effects, and the unknown balance between the costs of monitoring and prevention compared with the costs of potential harm, there is little current evidence to suggest that safeguarding human health should be a major reason for adopting such nutrient reduction strategies at this time.

The economics of nutrient reduction strategies and, in particular, their link to HABs have been poorly studied and is therefore inadequately understood. The economic approach should be to minimize the combined losses and management costs, but insufficient evidence currently exists to allow this to be conducted effectively. With concerns over public health at stake, the significant efforts that have gone into monitoring and regulating aquaculture and fisheries need to be maintained.

## Acknowledgements

The work described here is based in part on a project 'Harmful Algae, Nuisance Blooms and Anthropogenic Nutrient Enrichment' funded by the UK Department for Environment, Food and Rural Affairs (contract ME2208). The views expressed are those of the authors and not the Department. In addition KD was supported by the FP7 project Asimuth and funding from the NERC Shelf Seas Biogeochemistry and PURE Associates programmes. PJH was supported by University Grants Council of Hong Kong AoE project (AoE/P-04/0401). PH and LEF were funded by the US National Science Foundation (NSF) Award 1009106; LEF was funded in part by the European Regional Development Fund and European Social Fund (University of Exeter, Truro, Cornwall, UK). GM was supported by a NERC PhD studentship.

## References

- Anderson, D.M., 2000. Estimated Annual Economic Impacts from Harmful Algal Blooms (HABs) in the United States. Technical Report WHOI-2000-11.
- Anderson, D.M., 2003. The expanding global problem of harmful algal blooms. In: International Seminar on Nuclear War and Planetary Emergencies: 27th Session. World Scientific Publishing Co, New Jersey, pp. 372–393.
- Anderson, D.M., Anderson, P., Bricej, V., Cullen, J., Rensel, J., 2001. Monitoring and management strategies for harmful algal blooms in coastal waters. In: Asia Pacific Economic Program, Singapore, and Intergovernmental Oceanographic Commission Technical Series No. 59. IOC, Paris.
- Anderson, D.M., Glibert, P., Burkholder, J., 2002. Harmful algal blooms and eutrophication: nutrient sources, composition, and consequences. *Estuaries* 25, 704–726.
- Anderson, D.M., 1998. Physiology and bloom dynamics of toxic *Alexandrium* species, with emphasis on life cycle transitions. In: Anderson, D.M., Cembella, A.D., Hallegraeff, G. (Eds.), *The Physiological Ecology of Harmful Algal Blooms*. Springer-Verlag, Heidelberg, pp. 29–48.
- Anderson, D.M., 2004. Prevention, control and mitigation of harmful algal blooms: multiple approaches to HAB management. In: *Harmful Algae Management and Mitigation Asia-Pacific Economic Cooperation (Singapore): APEC Publication #204-MR-04.2*, pp. 123–130.
- Anderson, D.M., 2009. Approaches to monitoring, control and management of harmful algal blooms (HABs). *Ocean. Coast. Manag.* 52, 342.
- Anderson, D.M., Burkholder, J.M., Cochlan, W.P., Glibert, P.M., Gobler, C.J., Heil, C.A., Kudela, R., Parsons, M.L., Rensel, J.E.J., Townsend, D.W., Trainer, V.L., Vargo, G.A., 2008. Harmful algal blooms and eutrophication: examining linkages from selected coastal regions of the United States. *Harmful Algae* 8, 39–53.
- Anderson, D.M., Kaoru, Y., White, A.V., 2000. Economic Impacts from Harmful Algal Blooms (HABs) in the United States. Technical report WHOI-2000-11. Woods Hole Oceanographic Institute, Maine.
- Antia, N., Harrison, P.J., Oliveira, L., 1991. The role of dissolved organic nitrogen in phytoplankton nutrition, cell biology and ecology. *Phycology* 30, 1–89.
- Backer, L.C., Fleming, L.E., 2008. Epidemiologic tools to investigate oceans and public health. In: Walsh, P., Smith, W., Solo-Gabriele, H., Fleming, L. (Eds.), *Oceans and Human Health: Risks and Remedies from the Sea*. Elsevier, New York, pp. 201–218.
- Bean, J.A., Fleming, L.E., Kirkpatrick, B., Backer, L.C., Nierenberg, K., Reich, A., Cheng, Y.S., Wanner, A., Benson, J., Naar, J., Pierce, R., Abraham, W.M., Kirkpatrick, G., Hollenbeck, J., Zaias, J., Mendes, E., Baden, D.G., 2011. Florida red tide toxins (Brevetoxins) and longitudinal respiratory effects in asthmatics. *Harmful Algae* 10, 744–748.
- Black, K.D., 2001. Environmental Impacts of Aquaculture. Academic Press, Shellfield.
- Breton, E., Parent, J., Syste, E., Lancelot, C., 2006. Hydroclimatic modulation of diatom/*Phaeocystis* blooms in nutrient-enriched Belgian coastal waters (North Sea). *Limnol. Oceanogr.* 51, 1401–1409.
- Bruno, D., Dear, G., Seaton, D., 1989. Mortality associated with phytoplankton blooms amongst farmed *Atlantic Salmon, Salmo salar*. L., in Scotland. *Aquaculture*, 217–222.
- Burkholder, J.M., Glibert, P.M., Skelton, H.M., 2008. Mixotrophy, a major mode of nutrition for harmful algal species in eutrophic waters. *Harmful Algae* 8, 77–93.
- Cade, G.C., Hegeman, J., 2002. Phytoplankton in the Marsdiep at the end of the 20th century: 30 years monitoring biomass, primary production, and *Phaeocystis* blooms. *J. Sea Res.* 48, 97–110.
- Cadée, G.C., Hegeman, J., 1986. Seasonal and annual variation in *Phaeocystis pouchetii* (Haptophyceae) in the westernmost inlet of the Wadden Sea during the 1973 to 1985 period. *Netherlands J. Sea Res.* 20, 29–36.
- Capuzzo, E., 2011. Measuring and Modelling the Primary Production of a Sea Lough in Northern Ireland (PhD thesis).
- Cochlan, W.P., Herndon, J., Kudela, R.M., 2008. Inorganic and organic nitrogen uptake by the toxigenic diatom *Pseudo-nitzschia australis* (Bacillariophyceae). *Harmful Algae* 8, 111–118.
- Collos, Y., Vaquer, A., Laabir, M., Abadie, E., Laugier, T., Pastoureaud, A., Souchu, P., 2007. Contribution of several nitrogen sources to growth of *Alexandrium catenella* during blooms in Thau lagoon, southern France. *Harmful Algae* 6, 781–789.
- Davidson, K., Flynn, K.J., Cunningham, A., 1991. Relationships between photopigments, cell carbon, cell nitrogen and growth rate for a marine nanoflagellate. *J. Exp. Mar. Biol. Ecol.* 153, 87–96.
- Davidson, K., Flynn, K.J., Cunningham, A., 1992. Non-steady state ammonium-limited growth of the marine phytoflagellate, *Isochrysis galbana* Parke. *New Phytol.* 122, 433–438.
- Davidson, K., Gilpin, L.C., Hart, M.C., Fouilland, E., Mitchell, E., Calleja, I.A., Laurent, C., Miller, A.E.J., Leakey, R.J.G., 2007. The influence of the balance of inorganic and organic nitrogen on the trophic dynamics of microbial food webs. *Limnol. Oceanogr.* 52, 2147–2163.
- Davidson, K., Gurney, W.S.C., 1999. An investigation of non-steady-state algal growth. II. Mathematical modelling of co-nutrient-limited algal growth. *J. Plankton Res.* 21, 839–858.
- Davidson, K., Miller, P., Wilding, T.A., Shutler, J., Bresnan, E., Kennington, K., Swan, S., 2009. A large and prolonged bloom of *Karenia mikimotoi* in Scottish waters in 2006. *Harmful Algae* 8, 349–361.
- Davidson, K., Tett, P., Gowen, R., 2011. Harmful algal blooms. In: Hester, R., Harrison, R. (Eds.), *Marine Pollution and Human Health*, pp. 95–127.
- Droop, M.R., 1968. Vitamin B-12 and marine ecology. IV. The kinetics of uptake, growth, and inhibition in *Monochrysis lutheri*. *J. Mar. Biol. Assoc. UK.* 48, 689–733.
- Elser, J.J., Bracken, M.E.S., Cleland, E.E., Gruner, D.S., Harpole, W.S., Hillebrand, H., Ngai, J.T., Seabloom, E.W., Shurin, J.B., Smith, J.E., 2007. Global analysis of nitrogen and phosphorus limitation of primary producers in freshwater, marine and terrestrial ecosystems. *Ecol. Lett.* 10, 1135–1142.
- Fehling, J., Davidson, K., Bolch, C., Tett, P., 2006. Seasonality of *Pseudo-nitzschia* spp. (Bacillariophyceae) in western Scottish waters. *Mar. Ecol. Prog. Ser.* 323, 91–105.
- Fehling, J., Davidson, K., Bolch, C.J., Bates, S.S., 2004a. Growth and domoic acid production by *pseudo-nitzschia seriata* (Bacillariophyceae) under phosphate and silicate limitation. *J. Phycol.* 40, 674–683.
- Fehling, J., Green, D.H., Davidson, K., Bolch, C.J., Bates, S.S., 2004b. Domoic acid production by *Pseudo-nitzschia seriata* (Bacillariophyceae) in Scottish waters. *J. Phycol.* 40, 622–630.
- Ferreira, J.G., Andersen, J.H., Borja, A., Bricker, S.B., Camp, J., Cardoso da Silva, M., Garcés, E., Heiskanen, A.-S., Humborg, C., Ignatiades, L., Lancelot, C., Menesguen, A., Tett, P., Hoepffner, N., Claussen, U., 2011. Overview of eutrophication indicators to assess environmental status within the European Marine Strategy Framework Directive. *Estuar. Coast. Shelf Sci.* 93, 117–131.
- Fleming, L.E., Kirkpatrick, B., Backer, L.C., Walsh, C.J., Nierenberg, K., Clark, J., Reich, A., Hollenbeck, J., Benson, J., Cheng, Y.S., Naar, J., Pierce, R., Bourdelais, A.J., Abraham, W.M., Kirkpatrick, G., Zaias, J., Wanner, A., Mendes, E., Shalat, S., Hoagland, P., Stephan, W., Bean, J., Watkins, S., Clarke, T., Byrne, M., Baden, D.G., 2011. Review of florida red tide and human health effects. *Harmful Algae* 10, 224–233.
- Flynn, K.J., 2010. Ecological modelling in a sea of variable stoichiometry: dysfunctionality and the legacy of Redfield and Monod. *Prog. Oceanogr.* 84, 52–65.
- Flynn, K.J., Martin-Jézéquel, V., 2000. Modelling Si–N-limited growth of diatoms. *J. Plankton Res.* 22, 447–472.
- Foden, J., Devlin, M.J., Mills, D.K., Malcolm, S.J., 2010. Searching for undesirable disturbance: an application of the OSPAR eutrophication assessment method to marine waters of England and Wales. *Biogeochemistry* 106, 157–175.
- Geider, R., La Roche, J., 2002. Redfield revisited: variability of C:N:P in marine microalgae and its biochemical basis. *Eur. J. Phycol.* 37, 1–17.
- Gieskes, W.W.C., Letterm, S.C., Peletier, H., Edwards, M., Reid, P.C., 2007. *Phaeocystis* colony distribution in the North Atlantic Ocean since 1948, and interpretation of long-term changes in the *Phaeocystis* hotspot in the North Sea. *Biogeochemistry* 83, 49–60.
- Glibert, P.M., Azanza, R., Burford, M., Furuya, K., Abal, E., Al-Azri, A., Al-Yamani, F., Andersen, P., Anderson, D.M., Beardall, J., Berg, G.M., Brand, L., Bronk, D.,

- Brookes, J., Burkholder, J.M., Cembella, A., Cochlan, W.P., Collier, J.L., Collos, Y., Diaz, R., Doblin, M., Drennen, T., Dyhrman, S., Fukuyo, Y., Furnas, M., Galloway, J., Graneli, E., Ha, D.V., Hallegraeff, G., Harrison, J., Harrison, P.J., Heil, C.A., Heilmann, K., Howarth, R., Jauzein, C., Kana, A.A., Kana, T.M., Kim, H., Kudela, R., Legrand, C., Mallin, M., Mulholland, M., Murray, S., O'Neil, J., Pitcher, G., Qi, Y., Rabalais, N., Raine, R., Seitzinger, S., Salomon, P.S., Solomon, C., Stoecker, D.K., Usup, G., Wilson, J., Yin, K., Zhou, M., Zhu, M., 2008. Ocean urea fertilization for carbon credits poses high ecological risks. *Mar. Pollut. Bull.* 56, 1049–1056.
- Glibert, P.M., Harrison, J., Heil, C., Seitzinger, S., 2006. Escalating worldwide use of urea – a global change contributing to coastal eutrophication. *Biogeochemistry* 77, 441–463.
- Glibert, P.M., Legrand, C., 2006. The diverse nutrient strategies of harmful algae: focus on osmotrophy. In: Graneli, E., Turner, J. (Eds.), *Ecology of Harmful Algae*. Springer, Berlin, pp. 163–176.
- Glibert, P.M., Seitzinger, S.P., Heil, C.A., Burkholder, J.M., Parrow, M.W., Codispoti, L.A., Kelly, V., 2005. The role of eutrophication in the global proliferation of harmful algal blooms. *Oceanography* 18, 198–209.
- Glibert, P.M., Wazniak, C., Hall, M., Sturgis, B., 2007. Seasonal and interannual trends in nitrogen and brown tide in Maryland's coastal bays. *Ecol. Appl.* 17, S79–S87.
- Gowen, R.J., McKinney, A., Tett, P., Bresnan, E., Davidson, K., Harrison, P.J., Milligan, S., Mills, D.K., Silke, J., Crooks, A.M., 2012. Anthropogenic nutrient enrichment and blooms of harmful phytoplankton. *Oceanogr. Mar. Biol.* 50, 65–126.
- Gowen, R.J., Tett, P., Kennington, K., Mills, D.K., Shammon, T.M., Stewart, B.M., Greenwood, N., Flanagan, C., Devlin, M., Wither, A., 2008. The Irish Sea: Is it eutrophic? *Estuar. Coast. Shelf Sci.* 76, 239–254.
- Graneli, E., Johansson, N., Panosso, R., 1998. Cellular toxin contents in relation to nutrient conditions for different groups of *phycotoxins*. In: Reguera, B., Blanco, J., Fernandez, M., Wyatt, T. (Eds.), *Harmful Algae*. IOC, UNESCO, Paris, pp. 321–324.
- Gren, I., Elofsson, K., Jannke, P., 1997. Cost-effective nutrient reductions to the Baltic Sea. *Environ. Resour. Econ.* 10, 341–362.
- Hallegraeff, G.M., 1993. A review of harmful algal blooms and their appearance. *Phycologia* 32, 79–99.
- Hallegraeff, G.M., 2010. Ocean climate change, phytoplankton community responses, and harmful algal blooms: a formidable predictive challenge. *J. Phycol.* 46, 220–235.
- Harrison, P.J., Xu, J., Yin, K., Liu, H., Lee, J., Anderson, D., Hodgkiss, I., 2012. Is there a link between N:P ratios and red tides in Tolo Harbour, Hong Kong? In: Pagou, K., Hallegraeff, G. (Eds.), *Proceedings of 14th International Conference on Harmful Algae*. Hersonissos-Crete, Greece, pp. 90–92.
- Hays, G.C., Richardson, A.J., Robinson, C., 2005. Climate change and marine plankton. *Trends Ecol. Evol.* 20, 337–344.
- Heil, C.A., Glibert, P.M., Fan, C., 2005. *Prorocentrum minimum* (Pavillard) Schiller. A review of a harmful algal bloom species of growing worldwide importance. *Harmful Algae* 4, 449–470.
- Heisler, J., Glibert, P.M., Burkholder, J.M., Anderson, D.M., Cochlan, W., Dennison, W.C., Dortch, Q., Gobler, C.J., Heil, C.A., Humphries, E., Lewitus, A., Magnien, R., Marshall, H.G., Sellner, K., Stockwell, D.A., Stoecker, D.K., Suddleson, M., 2008. Eutrophication and harmful algal blooms: a scientific consensus. *Harmful Algae* 8, 3–13.
- Hickel, W., 1998. Temporal variability of micro- and nanoplankton in the German Bight in relation to hydrographic structure and nutrient changes. *ICES J. Mar. Sci.* 55, 600–609.
- Hinder, S.L., Hays, G.C., Brooks, C.J., Davies, A.P., Edwards, M., Walne, A.W., Gravenor, M.B., 2011. Toxic marine microalgae and shellfish poisoning in the British Isles: history, review of epidemiology, and future implications. *Environ. Health* 10, 54.
- Hoagland, P., 2008. From jubilees to halos: clarifying the economic effects of harmful algal blooms on commercial fisheries. *Am. Fish. Soc. Symp.* 64, 233–243.
- Hoagland, P., Anderson, D.M., Kaoru, Y., White, A., 2002. The economic effects of harmful algal blooms in the United States: estimates, assessment issues, and information needs. *Estuaries* 25, 677–695.
- Hoagland, P., Jin, D., Polansky, L., Kirkpatrick, B., Kirkpatrick, G., Fleming, L., Reich, A., Watkins, S., Ulmann, S., Backer, L.C., 2009. The costs of respiratory illnesses arising from Florida Gulf Coast *Karenia brevis* blooms. *Environ. Health Perspect.* 11, 1239–1243.
- Hoagland, P., Scatista, S., 2006. The economic effects of harmful algal blooms. In: Graneli, E., Turner, J. (Eds.), *Ecology of Harmful Algae*. Springer-Verlag, New York, pp. 391–402.
- Hodgkiss, I., Ho, K., 1997. Are changes in N: P ratios in coastal waters the key to increased red tide blooms? *Hydrobiologia* 352, 141–147.
- Holmes, L., 2012. The British Survey of Fertilizer Practice. Fertilizer use of farm crops for crop year 2012.
- Howarth, R.W., Marino, R., 2006. Nitrogen as the limiting nutrient for eutrophication in coastal marine ecosystems: evolving views over three decades. *Limnol. Ocean.* 51, 364–376.
- Humborg, C., Rahm, L., Conley, D.J., Tamminen, T., von Bodungen, B., 2008. Silicon and the Baltic Sea: long-term Si decrease in the Baltic Sea – a conceivable ecological risk? *J. Mar. Syst.* 73, 221–222.
- Imai, I., Yamaguchi, M., Hori, Y., 2006. Eutrophication and occurrences of harmful algal blooms in the Seto Inland Sea, Japan. *Plankt. Benthos Res.* 1, 71–84.
- Jin, D., Hoagland, P., 2008. The value of harmful algal bloom predictions to the nearshore commercial shellfish fishery in the Gulf of Maine. *Harmful Algae* 7, 772–781.
- Jin, D., Thunberg, E., Hoagland, P., 2008. Economic impact of the 2005 red tide event on commercial shellfish fisheries in New England. *Ocean. Coast. Manag.* 51, 420–429.
- John, E., Flynn, K., 2002. Modelling changes in paralytic shellfish toxin content of dinoflagellates in response to nitrogen and phosphorus supply. *Mar. Ecol. Prog. Ser.* 225, 147–160.
- Jones, H., 1997. A classification of mixotrophic protists based on their behaviour. *Freshw. Biol.* 37, 35–43.
- Kanoshina, I., Lips, U., Leppänen, J.-M., 2003. The influence of weather conditions (temperature and wind) on cyanobacterial bloom development in the Gulf of Finland (Baltic Sea). *Harmful Algae* 2, 29–41.
- Kim, H., 2010. An overview on the occurrences of harmful algal blooms (HABs) and mitigation strategies in Korean coastal waters. In: *Coastal Environmental and Ecosystem Issues of the East China Sea*, pp. 121–131.
- Kite-Powell, H.L., Fleming, L.E., Backer, L.C., Faustman, E.M., Hoagland, P., Tsuchiya, A., Younglove, L.R., Wilcox, B.A., Gast, R.J., 2008. Linking the oceans to public health: current efforts and future directions. *Environ. Health* 7 (suppl. 2), S6.
- Lancelot, C., Thieu, V., Polard, A., Garnier, J., Billen, G., Hecq, W., Gypens, N., 2011. Cost assessment and ecological effectiveness of nutrient reduction options for mitigating *Phaeocystis* colony blooms in the Southern North Sea: an integrated modeling approach. *Sci. Total Environ.* 409, 2179–2191.
- Leong, S.C.Y., Murata, A., Nagashima, Y., Taguchi, S., 2004. Variability in toxicity of the dinoflagellate *Alexandrium tamarense* in response to different nitrogen sources and concentrations. *Toxicol.* 43, 407–415.
- Lønborg, C., Davidson, K., Alvarez-Salgado, X.A., Miller, A.E.J., 2009. Bioavailability and bacterial degradation rates of dissolved organic matter in a temperate coastal area during an annual cycle. *Mar. Chem.* 113, 219–226.
- Loureiro, S., Garcés, E., Fernández-Tejedor, M., Vaqué, D., Camp, J., 2009. *Pseudo-nitzschia* spp. (Bacillariophyceae) and dissolved organic matter (DOM) dynamics in the Ebro Delta (Alfacs Bay, NW Mediterranean Sea). *Estuar. Coast. Shelf Sci.* 83, 539–549.
- McKee, D., Fleming, L.E., Tamer, R., Weisman, R., Blythe, D., 2001. Ciguatera fish poisoning reporting by physicians in an endemic area. In: Hallegraeff, G., Blackburn, S., Bolch, C., Lewis, R. (Eds.), *Harmful Algal Blooms 2000*. UNESCO/IOC, Paris, pp. 451–453.
- Minnhagen, S., Kim, M., Salomon, P., Yih, W., Graneli, E., Park, M., 2011. Active uptake of kleptoplastids by *Dinophysis caudata* from its ciliate prey *Myrionecta rubra*. *Aquat. Microb. Ecol.* 62, 99–108.
- Montagnes, D.J.S., Barbosa, A.B., Boenigk, J., Davidson, K., Jürgens, K., Macek, M., Parry, J.D., Roberts, E.E., Simek, K., 2008. Selective feeding behaviour of key free-living protists: avenues for continued study. *Aquat. Microb. Ecol.* 53, 83–98.
- Moore, S.K., Trainer, V.L., Mantua, N.J., Parker, M.S., Laws, E.A., Backer, L.C., Fleming, L.E., 2008. Impacts of climate variability and future climate change on harmful algal blooms and human health. *Environ. Health* 7 (suppl. 2), S4.
- Morgan, K.L., Larkin, S.L., Adams, C.M., 2009. Firm-level economic effects of HABs: a tool for business loss assessment. *Harmful Algae* 8, 212–218.
- Morgan, K.L., Larkin, S.L., Adams, C.M., 2010. Red tides and participation in marine-based activities: estimating the response of Southwest Florida residents. *Harmful Algae* 9, 333–341.
- Murata, A., Leong, S.C.Y., Nagashima, Y., Taguchi, S., 2006. Nitrogen:Phosphorus supply ratio may control the protein and total toxin of dinoflagellate *Alexandrium tamarense*. *Toxicol.* 48, 683–689.
- Nishikawa, T., Hori, Y., Nagai, S., Miyahara, K., Nakamura, Y., Harada, K., Tanda, M., Madabe, T., Tada, K., 2010. Nutrient and phytoplankton dynamics in Harima-Nada, Eastern Seto Inland Sea, Japan during a 35-year period from 1973 to 2007. *Est. Coasts* 33, 417–427.
- Nunes, P., van den Bergh, J., 2004. Can people value protection against invasive marine species? Evidence from a joint TC–CV survey in the Netherlands. *Env. Res. Econ.* 28, 517–532.
- Officer, C., Ryther, J., 1980. The possible importance of silicon in marine eutrophication. *Mar. Ecol. Prog. Ser.* 3, 83–91.
- Okamoto, K., Fleming, L.E., 2005. Algae. In: Wexler, P. (Ed.), *Encyclopedia of Toxicology*. Oxford University Press, Oxford, pp. 68–76.
- Olascoaga, M., Beron Vera, F., Brand, L., Kocak, H., 2008. Tracing the early development of harmful algal blooms on the West Florida shelf with the aid of Lagrangian coherent structures. *J. Geophys. Res.-Oceans* 113, C12014.
- Pan, Y., Subba Rao, D., Mann, K.H., RG, B., Pocklington, R., 1996. Effects of silicate limitation on production of domoic acid, a neurotoxin, by the diatom *Pseudo-nitzschia multiseries*. I. Batch Cult. *Stud. Mar.* 131, 225–233.
- Park, M., Kim, S., Kim, H., Myung, G., Kang, Y., Yih, W., 2006. First successful culture of the marine dinoflagellate *Dinophysis acuminata*. *Aquat. Microb. Ecol.* 45, 101–106.
- Parsons, G., Morgan, A., Whitehead, J., Haab, T., 2006. The welfare effects of *Pfiesteria*-related fish kills: a contingent behavior analysis of seafood consumers. *Ag. Res. Econ. Rev.* 35, 348–356.
- Pete, R., Davidson, K., Hart, M.C., Gutierrez, T., Miller, A.E.J., 2010. Diatom derived dissolved organic matter as a driver of bacterial productivity: the role of nutrient limitation. *J. Exp. Mar. Bio. Ecol.* 391, 20–26.
- Phillipart, C., Beukema, J., Cadée, G.C., Dekker, R., Goedhart, P.W., van Iperen, J., Leopold, M.F., Herman, P.M.J., 2007. Impacts of nutrient reduction on coastal communities. *Ecosystems* 10, 96–119.
- Probyn, T.A., Bernard, S., Pitcher, G.C., Pienaar, R.N., 2010. Ecophysiological studies on *Aureococcus anophagefferens* blooms in Saldanha Bay, South Africa. *Harmful Algae* 9, 123–133.

- Reynolds, C.S., 1999. Non-determinism to probability, or N:P in the community ecology of phytoplankton. *Arch. Hydrobiol.* 146, 23–25.
- Richardson, K., 1997. Harmful or exceptional phytoplankton blooms in the marine ecosystem. *Adv. Mar. Biol.* 31.
- Riegman, R., Noordeloos, A.A.M., Cadée, G., 1992. *Phaeocystis* blooms and eutrophication of the continental coastal zones of the North Sea. *Mar. Biol.* 112, 479–484.
- Scatania, S., 2004. The role of respondents' experience in contingent valuation analysis: the case of harmful algal blooms and European Union coastal tourism. In: 13th Annual EAERE Conference. Budapest.
- Scatasta, S., Stolte, W., Graneli, E., Weikard, H., van Ireland, E., 2003. ECOHARM: the socio-economic impact of harmful algal blooms in European marine waters. In: Contract No. EVK3-CT-2001–80003. Environmental Economics and Natural Resources Group. Wageningen University, The Netherlands.
- Sinclair, G., Kamykowski, D., Glibert, P.M., 2009. Growth, uptake, and assimilation of ammonium, nitrate, and urea, by three strains of *Karenia brevis* grown under low light. *Harmful Algae* 8, 770–780.
- Smayda, T.J., 1990. Novel and nuisance phytoplankton blooms in the sea – evidence for a global epidemic. In: Graneli, E., Sundstrom, B., Edler, L., Anderson, D. (Eds.), *Toxic Marine Phytoplankton*. Elsevier, New York, pp. 29–40.
- Smayda, T.J., 2007. Reflections on the ballast water dispersal–harmful algal bloom paradigm. *Harmful Algae* 6, 601–622.
- Soderqvist, T., 1998. Why give up money for the Baltic Sea? – Motives for people's willingness (or reluctance) to pay. *Env. Res. Econ.* 12, 249–254.
- Solomon, C., Collier, J., Berg, G., Glibert, P., 2010. Role of urea in microbial metabolism in aquatic systems: a biochemical and molecular review. *Aquat. Microb. Ecol.* 59, 67–88.
- Solomon, C., Glibert, P., 2008. Urease activity in five phytoplankton species. *Aquat. Microb. Ecol.* 52, 149–157.
- Sournia, A., 1995. Red tide and toxic marine phytoplankton of the world ocean: an inquiry into biodiversity, in: *Harmful Marine Algal Blooms. Proceedings of the 6th International Conference on Toxic Marine Phytoplankton October 1993, Nantes, France*, pp. 103–112.
- Sterner, R.W., Elser, J.J., 2002. *Ecological Stoichiometry: the Biology of Elements from Molecules to the Biosphere*. Princeton University Press.
- Stewart, J., Fleming, L.E., Fleisher, J., Abdelzahir, A., Lyons, M., 2011. Waterborne pathogens. In: Hester, R., Harrison, R. (Eds.), *Marine Pollution and Human Health, Issues in Environmental Science and Technology*. Royal Society of Chemistry, London, pp. 25–67.
- Stoecker, D.K., 1998. Conceptual models of mixotrophy in planktonic protists and some ecological and evolutionary implications. *Eur. J. Protistol.* 34, 281–290.
- Stumpf, R.P., Tomlinson, M.C., Calkins, J.A., Kirkpatrick, B., Fisher, K., Nierenberg, K., Currier, R., Wynne, T.T., 2009. Skill assessment for an operational algal bloom forecast system. *J. Mar. Syst.* 76, 151–161.
- Taroncher-Oldenburg, G., Kulis, D.M., Anderson, D.M., 1999. Coupling of saxitoxin biosynthesis to the G1 phase of the cell cycle in the dinoflagellate *Alexandrium fundyense*: temperature and nutrient effects. *Nat. Toxins* 7, 207–219.
- Taylor, T., Luongo, A., 2009. Valuation of Marine Ecosystem Threshold Effects: Application of Choice Experiments to Value Algal Bloom in the Black Sea Coast of Bulgaria. Working paper 7/09. Department of Economics. University of Bath.
- Tett, P., Gowen, R.J., Grantham, B., Jones, K., Miller, B.S., 1986. The phytoplankton ecology of the firth of Clyde sea lochs Striven and Fyne. *Proc. R. Soc. Edinb. B* 90, 223–238.
- Tett, P., Hydes, D.J., Sanders, R., 2003. Influence of nutrient biogeochemistry on the ecology of north-west European shelf seas. In: *Biogeochemistry of Marine Systems*. Academic Press, Sheffield, pp. 293–363.
- Tilman, D., 1977. Resource competition between plankton algae: an experimental and theoretical approach. *Ecology* 58, 338–348.
- Trainer, V.L., Leberhart, B.-T., Wekeu, J., Adams, V., Hanson, L., Cox, F., Dowell, J., 2003. Paralytic shellfish toxins in Puget sound, Washington State. *J. Shellfish Res.* 22, 213–223.
- Vahtera, E., Conley, D.J., Gustafsson, B.G., Kuosa, H., Pitkänen, H., Savchuk, O.P., Tamminen, T., Viitasalo, M., Voss, M., Wasmund, N., Wulff, F., 2007. Internal ecosystem feedbacks enhance nitrogen-fixing cyanobacteria blooms and complicate management in the Baltic Sea. *Ambio* 36, 186–194.
- Van Dolah, F., 2000. Marine algal toxins. *Env. Health Persp.* 108, 133–141.
- Vargo, G.A., Heil, C.A., Fanning, K.A., Dixon, L.K., Neely, M.B., Lester, K., Ault, D., Murasko, S., Havens, J., Walsh, J., Bell, S., 2008. Nutrient availability in support of *Karenia brevis* blooms on the central West Florida Shelf: what keeps *Karenia* blooming? *Cont. Shelf Res.* 28, 73–98.
- Watkins, S.M., Reich, A., Fleming, L.E., Hammond, R., 2008. Neurotoxic shellfish poisoning. *Mar. Drugs* 6, 431–455.
- Wells, M.L., Trick, C.G., Cochlan, W.P., Hughes, M.P., Trainer, V.L., 2005. Domoic acid: the synergy of iron, copper, and the toxicity of diatoms. *Limnol. Oceanogr.* 50, 1908–1917.
- Wessells, C., Miler, C., Brooks, P., 1995. Toxic algae contamination and demand for shellfish: a case study of demand for mussels in Montreal. *Mar. Res. Econ.* 10, 143–159.
- Wong, K.T.M., Lee, J.H.W., Harrison, P.J., 2009. Forecasting of environmental risk maps of coastal algal blooms. *Harmful Algae* 8, 407–420.
- Xu, J., Ho, A.Y.T., He, L., Yin, K., Hung, C., Choi, N., Lam, P.K.S., Wu, R.S.S., Anderson, D.M., Harrison, P.J., 2012. Effects of inorganic and organic nitrogen and phosphorus on the growth and toxicity of two *Alexandrium* species from Hong Kong. *Harmful Algae* 16, 89–97.
- Xu, J., Yin, K., Liu, H., Lee, J.H.W., Anderson, D.M., Ho, A.Y.T., Harrison, P.J., 2010. A comparison of eutrophication impacts in two harbours in Hong Kong with different hydrodynamics. *J. Mar. Syst.* 83, 276–286.
- Yamamoto, T., 2003. The Seto Inland Sea–eutrophic or oligotrophic? *Mar. Pollut. Bull.* 47, 37–42.
- Zaia, J., Backer, L.C., Fleming, L.E., 2010. Harmful algal blooms (HABs). In: Rabinowitz, P., Conti, L. (Eds.), *Human-animal Medicine: a Clinical Guide to Toxins, Zoonoses, and Other Shared Health Risks*. Elsevier, New York, pp. 91–104.